Attorney Docket No. 09032.0001
Customer Number 22,852

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Knut BRABRAND	)	Group Art Unit: 3737
	)	
Application No.: 10/725,431	)	Examiner:
	)	
Filed: December 3, 2003	)	
	)	
For: RESPIRATION MONITOR	)	
	)	

MAIL STOP MISSING PARTS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

CLAIM FOR PRIORITY

Under the provisions of 35 U.S.C. § 119, Applicant hereby claims the benefit of the filing date of United Kingdom Patent Application No. 0228189.7, filed December 3, 2002, for the above-identified U.S. patent application.

In support of this claim for priority, enclosed is one certified copy of the priority application.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: May 3, 2004

By: _____
Ernest F. Chapman
Reg. No. 25,961

EFC/FPD/gah
Enclosures

The Patent Office
Concept House
Cardiff Road
Newport
South Wales
NP10 8QQ

I, the undersigned, being an officer duly authorised in accordance with Section 74(1) and (4) of the Deregulation & Contracting Out Act 1994, to sign and issue certificates on behalf of the Comptroller-General, hereby certify that annexed hereto is a true copy of the documents as originally filed in connection with the patent application identified therein.

In accordance with the Patents (Companies Re-registration) Rules 1982, if a company named in this certificate and any accompanying documents has re-registered under the Companies Act 1980 with the same name as that with which it was registered immediately before re-registration save for the substitution as, or inclusion as, the last part of the name of the words "public limited company" or their equivalents in Welsh, references to the name of the company in this certificate and any accompanying documents shall be treated as references to the name with which it is so re-registered.

In accordance with the rules, the words "public limited company" may be replaced by p.l.c., plc, P.L.C. or PLC.

Re-registration under the Companies Act does not constitute a new legal entity but merely subjects the company to certain additional company law rules.

Signed P. Mahoney

Dated 23 December 2003

040EC02 E768235-1 D00027
P01/7700 0.00-0228189.7

Patents Form 1/77

Pa Act 1977
(Rule 16)

The Patent Office

1/77

Request for grant of a patent

(See the notes on the back of this form. You can also get an explanatory leaflet from the Patent Office to help you fill in this form)

THE PATENT OFFICE
J
-3 DEC 2002
LONDON

The Patent Office
Cardiff Road
Newport
Gwent NP9 1RH

1. **Your reference** — 31.32.79685

2. **Patent application number** *(The Patent Office will fill in this part)* — 0228189.7 — 03 DEC 2002

3. **Full name, address and postcode of the or of each applicant** *(underline all surnames)*

NeoRad AS
Parkveien 55
0256 Oslo
Norway

Patents ADP number *(if you know it)* 08520207001

If the applicant is a corporate body, give country/state of incorporation Norway

4. **Title of the invention** — Respiration Monitor

5. **Name of your agent** *(if you have one)*

Frank B. Dehn & Co.

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

179 Queen Victoria Street
London
EC4V 4EL

Patents ADP number *(if you know it)* 166001

6. **If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and** *(if you know it)* **the or each application number**

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. **If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application**

Number of earlier application	Date of filing *(day / month / year)*

8. **Is a statement of inventorship and of right to grant of a patent required in support of this request?** *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

yes

9.	**Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document**	
	Continuation sheets of this form	0
	Description	11
	Claim(s)	3
	Abstract	1
	Drawing(s)	4 + 4
10.	**If you are also filing any of the following, state how many against each item.**	
	Priority documents	0
	Translations of priority documents	0
	Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	1
	Request for preliminary examination and search *(Patents Form 9/77)*	
	Request for substantive examination *(Patents Form 10/77)*	
	Any other documents *(please specify)*	0
11.	**I/We request the grant of a patent on the basis of this application.**	
	Signature	**Date** 3 December 2002
12.	**Name and daytime telephone number of person to contact in the United Kingdom**	Robert Jackson 020 7206 0600

Warning

After an application for a patent has been filed, the Comptroller of the Patent Office will consider whether publication or communication of the invention should be prohibited or restricted under Section 22 of the Patents Act 1977. You will be informed if it is necessary to prohibit or restrict your invention in this way. Furthermore, if you live in the United Kingdom, Section 23 of the Patents Act 1977 stops you from applying for a patent abroad without first getting written permission from the Patent Office unless an application has been filed at least 6 weeks beforehand in the United Kingdom for a patent for the same invention and either no direction prohibiting publication or communication has been given, or any such direction has been revoked.

Notes

a) *If you need help to fill in this form or you have any questions, please contact the Patent Office on 0645 500505.*
b) *Write your answers in capital letters using black ink or you may type them.*
c) *If there is not enough space for all the relevant details on any part of this form, please continue on a separate sheet of paper and write "see continuation sheet" in the relevant part(s) of the form. Any continuation sheet should be attached to this form.*
d) *If you have answered 'Yes', Patents Form 7/77 will need to be filed.*
e) *Once you have filled in the form you must remember to sign and date it.*
f) *For details of the fee and ways to pay please contact the Patent Office.*

79685

Respiration Monitor

The present invention relates to a non-invasive method and apparatus for monitoring the degree of inspiration of a medical or surgical patient's lungs.

In many circumstances (e.g. when performing biopsies or radiotherapy), it is desirable to precisely locate a target area of a lung or of an organ in the upper abdomen. For example, in order to perform a lung biopsy, pre-operative CT images may be generated. These are then used to determine how the biopsy needle should be inserted in order to reach its target. After the needle has been inserted, fresh CT images may be generated in order to check the position of the needle. If necessary, this can then be corrected and the procedure repeated in an iterative manner.

During such a CT guided puncture, several parameters are of great importance in order to hit the target, e.g. insertion of the needle with the correct angle, needle deflection at various tissue interfaces and patient cooperation, including respiratory control. Lesions in the lungs, particularly in the lower parts, and also in the upper abdominal area move with respiration. The degree of respiratory movement is greater in the lower parts of the lung and the upper part of the abdomen. Other organs and tissues move to some extent with respiration.

Although some x-ray based imaging techniques can be used in real-time, it is not desirable to continuously monitor a biopsy using x-rays because of the well known risks associated with exposure to such radiation. Magnetic implements cannot be used during MRI scans because of the high magnetic field used.

Conventionally, the patient is asked to hold his breath when the CT scan takes place. He is then asked to hold his breath at the same level of inspiration during

puncture. However, it will be appreciated that it is difficult for the patient to reproduce the same degree of inspiration. Consequently, the images may not accurately reflect the position of the target within the patient. Thus, an objective means of monitoring the level of inspiration could improve the puncture accuracy because the operator would have better control over the movement of the target along the longitudinal body axis (the z-direction).

US 6,110,112 discloses a medical guide apparatus for breath-coordinated puncturing of the body. In this apparatus, a reference point is located which will be visible in both an ultrasound scan and in an MRI or CT scan. The arrangement is such that the location of the reference point will vary with respiration in the same manner as the target point. The target (which shows up in only the MRI or CT scan) can then be located by calculating its position relative to the reference point. The practitioner must calculate the relative displacements in the x, y and z-axes of the target point from the reference point.

The apparatus of US 6,110,112 consists of an ultrasound applicator with a puncture instrument attached thereto. The relative displacement between the ultrasound applicator and the puncture instrument is variable. The practitioner therefore sets the relative displacement of the puncture instrument from the ultrasound applicator such that the puncture instrument is directed at the target. Then, the practitioner locates the reference point with the ultrasound applicator and performs the puncture. This method requires that the reference point used moves in exactly the same way as the target area throughout the respiration cycle. It also requires a cumbersome apparatus to be mounted above the patient after the CT or MRI scan has been performed.

There is a similar problem of z-direction movement

associated with radiation therapy of a tumor. If the tumor is in the lung or upper part of the abdomen, it may move in and out of the focus of the radiation beam as the lungs expand and contract. The current method of overcoming this problem is to choose the area to be irradiated to be large enough to cover the tumor during its respiratory movement. This inevitably results in the irradiation of non-cancerous tissue. The inventors have therefore recognized that a device that can monitor and send information about the respiration to a radiation unit would be desirable. This could enable a radiation unit to map the radiation beam as a function of the patient respiration and thus trigger the radiation unit to only radiate when the tumor is in focus.

According to the invention there is provided a method of determining the degree of lung inspiration in a patient comprising the step of non-invasively detecting the position of the patient's diaphragm.

Thus, the invention is based on the recognition that the diaphragm provides an effective and measurable reference point that may be used to define lung inspiration.

The invention may thus be used to assist in image-guided procedures as discussed above. The diaphragm position may therefore be used to define the degree of lung inspiration when an image of the patient is generated and the method may further comprise the step of reproducing that degree of lung inspiration in order to perform a medical or surgical procedure on the patient based on that image.

For example, diaphragm position may first be determined and then, whilst the patient holds his breath, images may be generated. Subsequently, the degree of lung inspiration may be substantially reproduced by the patient inhaling until the previously determined diaphragm position is achieved. The desired procedure is then carried out whilst the patient holds

his breath.

Although diaphragm position could be determined using a number of techniques, particularly non-invasive imaging techniques, it is preferred to use ultrasound. This does not subject the patient to ionizing radiation and is convenient to use. Although ultrasound cannot image certain body structures it provides a very effective way to determine the position of the diaphragm.

A conventional hand-held ultrasound probe could be used to scan the patient's abdomen. However, this would still require a reference point to define the diaphragm's position and it would be difficult to monitor movement of the diaphragm.

Thus, according to a preferred aspect of the invention there is provided a method of monitoring the degree of lung inspiration in a patient comprising providing an array of ultrasound transducer elements on the patient extending over the lung sinus, wherein the position of the diaphragm is determined based upon the signals received by the individual transducer elements.

The invention makes use of the fact that air has a very high acoustic impedance compared to non-aerated tissue (tissue not containing air). During inspiration, as the lung expands downwards and fills with air, the lung sinus opens up. The acoustic impedance of the lung sinus is thus increased. The opposite takes place during expiration. As a consequence, transducer elements located adjacent to aerated tissue will provide very distinct outputs compared to those adjacent to non-aerated tissue. In this way the invention allows accurate real time monitoring of the position of the diaphragm.

As the transducer elements are adapted to extend over the lung sinus, they may extend from the upper abdomen of a patient to the lower chest, the upper abdomen and the lower chest meeting at the lung sinus

and being divided from one another by the diaphragm.

The invention also extends to an apparatus for performing such a method and therefore, viewed from another aspect, the invention provides an apparatus for monitoring the degree of lung inspiration in a patient comprising an array of ultrasound transducer elements for placing on the patient to extend over the lung sinus, wherein the position of the diaphragm may be determined based upon signals received by the individual transducer elements.

The array preferably comprises a series of ultrasound transducer elements (more preferably low cost disposable transducer elements)that is placed in a line in the z-direction over the lung sinus. The array is preferably fixed to the patient's skin in a lower intercostal space using an adhesive. In accordance with standard practice, a coupling medium (ultrasound gel) should preferably be applied to the patient's skin under the transducer elements.

In preferred forms of the invention the transducer array may indicate its own proper placement by giving feedback to the user. Thus, in one preferred method, the array of ultrasound transducer elements is placed over the patient's lower chest and/or upper abdomen and is moved to a desired location over the lung sinus using feedback from the ultrasound transducer elements.

In one preferred embodiment, the array of transducer elements is made long enough to extend across the full extent of movement of a patient's diaphragm, i.e. to cover a patient's full breathing range. In an alternative embodiment however, the array of transducer elements may be shorter than the full breathing range of a patient, so as for example to cover 50% of a patient's full breathing range. In one possible embodiment, a single transducer element could be used rather than an array but this would require cooperation from a patient to hold their breath while the diaphragm was located and

the transducer element positioned thereon. Further, it is believed that the use of a single transducer element would not be as accurate as it would be very difficult to position the transducer element directly on the edge of the diaphragm. More preferably therefore, at least two transducer elements are used. This has the advantage that a transducer element can be placed on either side of the diaphragm to give a user the certainty that the diaphragm is located between the two elements when the difference in reading obtained by the two elements is sufficiently high.

Although the transducer array of the present invention need only be a one dimensional array in the direction of the longitudinal (z) axis of the patient, a two dimensional array or a plurality of two dimensional arrays could be used if required to more accurately measure the exact two or three dimensional shape and location of an aerated cavity inside a patient.

In operation, the transducer array will start monitoring the movement of the lung sinus; each transducer element will detect a change in impedance as the patient breathes. The output from the transducer array can be registered for later use or constantly fed to a monitor or device.

In a simple case the outputs from the transducer elements may be regarded as essentially digital - in simple terms the output from each may be regarded as either indicating air (above the diaphragm) or indicating tissue (on or below the diaphragm). These outputs may then be fed to a processor that determines the position of the "step" from one to the other. This will correspond to diaphragm position. An output may then be made on a display, for example as a numerical value on an arbitrary scale.

In a more sophisticated embodiment the measured acoustic impedance from each transducer element is used as an input to the processor. Impedance may then be

processed as a function that varies with the z-direction. The impedance values may, for example, be plotted on a visual display and a curve fitted to them. The diaphragm position will correspond to the point of greatest gradient. This can either be determined visually by an operator or calculated and presented as a position-value.

Using this apparatus it is possible to monitor the position of the lung sinus and thereby the diaphragm with great accuracy in real time. Procedures such as lung biopsies may therefore be performed with greater ease.

Moreover, in the context of radiotherapy, the apparatus may be coupled to a source of radiation and be arranged to trigger that source to emit radiation when the diaphragm is at a specific position. In this way, the radiation need only be directed at the patient when it is directly focused on its target. In an alternative and particularly preferred form of the invention, the direction of the radiation beam may be controlled to follow the movement of the target based on the determined position of the diaphragm.

In one such embodiment, the location of the tumor is measured at several different levels of inspiration and the path of the tumor throughout a normal breathing cycle is calculated as a function of diaphragm position. The radiation source is mounted on a tracking device that is controlled by the control unit to direct the radiation towards the calculated position of the tumor based on the current measurement of diaphragm position.

Furthermore, the inventors have recognized that when monitoring the respiratory status of seriously ill patients, e.g. in the intensive care unit (ICU) it would be useful to measure the position of the diaphragm by means of the present invention. This would give important information about the quality of respiration that is not available with the techniques currently used

in the ICU.

A preferred embodiment of the present invention will now be described, by way of example only, with reference to the accompanying drawings in which:-

Fig. 1 shows a schematic representation of an embodiment of the invention using an array of ultrasound transducer elements to detect the location of a patient's diaphragm;

Fig. 2 shows the diaphragm in a contracted state (after inspiration);

Fig. 3 illustrates output from the embodiment in the form of a graph illustrating acoustic impedance plotted against the z-direction with the diaphragm in a contracted state;

Fig. 4 corresponds to Fig. 2 but shows the diaphragm in a relaxed state(after expiration);

Fig. 5 corresponds to Fig. 3 but shows an impedance signal corresponding to the diaphragm state shown in Fig. 4;

Fig. 6 shows a system for implementing the embodiment of Figure 1 illustrating how the invention may be utilised.

For the sake of clarity, the present invention will now be described with reference to a CT guided puncture operation. However, it will be understood that, as discussed above, embodiments of the invention can also be used in the fields of radiation therapy and other aspects of respiration monitoring.

Fig. 1 shows a respiration monitoring apparatus in accordance with the present invention. A patient 1 having a lung 2 and an abdomen 3 being separated therefrom by a diaphragm 4 is fitted with an ultrasound transducer array 5 positioned approximately centrally over the lung sinus 6 prior to being given a CT or MRI scan. The transducer array 5 consists of a plurality of individual transducer elements 7 that span at least a part of the region of diaphragm movement i.e. from a

relaxed state to a contracted state. In one embodiment, the transducer array is adapted to span the entire region of diaphragm movement. In alternative embodiments however, it can be adapted to span only 75%, 50% or 25% of the region of diaphragm movement respectively. In further possible embodiments, the array can be adapted to span from 1% to 15% or from 1% to 20% or from 1% to 25% of the region of diaphragm movement respectively. In a further possible alternative, the array consists of only one single ultrasound transducer element which is positioned at a particular point in the cycle of movement of the diaphragm in use.

Each individual transducer element 7 emits an ultrasound pulse and then detects its echo in the known manner. Because air has a much higher acoustic impedance than tissue, the reflection of the ultrasound beam is much more pronounced when the lung is insonated. Thus, the strength of signal received will be much higher when the pulse is reflected from an aerated space than when the pulse is reflected by tissue..

By measuring the strength of the receiving signal, i.e. the degree to which the transducers are receiving from air and from tissue, it is possible to determine to a high degree of accuracy the position of the patient's diaphragm.

In order to avoid interference between adjacent transducer elements, their pulses are phased so as not to occur simultaneously. However, because the duration of each pulse is very short, output that is effectively in real-time is produced.

As shown in Figure 6, the measured acoustic impedance from each transducer element is used as an input to a processor 8. Impedance may then be processed as a function that varies in the z-direction. The impedance values are then plotted on a visual display 9 and a curve fitted to them. The diaphragm position will

correspond to the point of greatest gradient. This is calculated by the processor 8, highlighted on the display 9 and presented as a numerical position-value, also on the display 9.

After the patient 1 has been fitted with the transducer array 5, a CT or an MRI scan is performed on the patient to determine the precise location of the target (e.g. a lesion to be punctured). During the scan, the patient is required to hold his breath so that a clear image is produced with the lungs in one position. While the scan is being performed and while the patient is holding his or her breath, the exact position of the diaphragm is presented on the display and the position-value is noted.

The image from the scan is used to calculate the depth and angle at which a needle must be inserted for the lesion to be punctured. When the operator is ready to perform the puncture, the patient is asked to inhale until the display indicates that the diaphragm is in the same position as it was when the scan was performed. If the patient inhales too much and the transducer array indicates that the level of inspiration is greater than that held during the scan, the operator can instruct the patient to exhale a little. If necessary, the patient can relax and inhale again until the operator is happy with the position of the diaphragm.

In this way, the operator can be sure that the lesion is at the same position within the patient as it is shown in the CT or MR image while he or she performs the puncture. In the case of CT, the location of the needle may, however, still be checked by means of a further scan.

As described above, the apparatus of the present invention can also be used to improve radiotherapy treatments by reducing the area that needs to be irradiated. The basic procedure described above is employed, however, the embodiment is modified to provide

a control output from the processor for controlling a source of radiation.

After the location of the tumor within the patient has been determined from the scan image, a radiation source is aimed at that location. This is connected to the control output such that the radiation source only emits when triggered to do so by the output signal from the processor.

The patient is allowed to breathe continuously throughout the radiation treatment. Meanwhile, the processor uses the outputs from the transducer array to continuously monitor the position of the diaphragm. When its position corresponds to the position that was determined during the scan, the processor sends a signal to trigger the radiation source to irradiate the target area of the patient. Thus, the area of the patient that needs to be irradiated can be significantly reduced because the location of the target can be determined to a much greater accuracy.

Claims:

1. A method of determining the degree of lung inspiration in a patient comprising the step of non-invasively detecting the position of the patient's diaphragm.

2. A method as claimed in claim 1, wherein the diaphragm position is used as a reference point to define the degree of lung inspiration when an image of the patient is generated and further comprising the step of reproducing that degree of lung inspiration in order to perform a medical or surgical procedure on the patient based on that image.

3. A method as claimed in claim 2, wherein diaphragm position is first determined whilst the patient holds his breath and images are generated simultaneously therewith, the degree of lung inspiration subsequently being reproduced by the patient inhaling or inhaling and exhaling until the previously determined diaphragm position is achieved and the desired procedure being then carried out whilst the patient holds his breath.

4. A method as claimed in any preceding claim, wherein the diaphragm position is determined by means of ultrasound.

5. A method as claimed in any preceding claim, comprising providing an array of ultrasound transducer elements on the patient extending over the lung sinus, wherein the position of the diaphragm is determined based upon the signals received by the individual transducer elements.

6. A method as claimed in claim 5, wherein the array

of ultrasound transducer elements is placed on the patient's lower chest and/or upper abdomen and is moved into a desired position over the lung sinus using feedback from the ultrasound transducer elements.

7. An apparatus for monitoring the position of a patient's diaphragm comprising an array of ultrasound transducer elements for placing on the patient to extend over the lung sinus, wherein the position of the diaphragm may be determined based upon signals received by the individual transducer elements.

8. An apparatus as claimed in claim 7, wherein the array of transducer elements is a one-dimensional array in the direction of the longitudinal (z) axis of the patient.

9. An apparatus as claimed in any of claims 6 to 8, wherein the measured acoustic impedance from each transducer element is used as an input to a processor and acoustic impedance may be processed to provide a function that varies with the movement of the diaphragm in the z-direction.

10. A method of performing a biopsy using the method or apparatus of any preceding claim.

11. A method of radiotherapy comprising providing a source of radiation and directing it at a target area of a patient, wherein the emission of the radiation beam is triggered by means of an apparatus according to any of claims 7 to 9.

12. A method of radiotherapy comprising providing a source of radiation and directing it at a target area of a patient, wherein the emission of the radiation beam may be controlled to follow the movement of the target

based on the position of the diaphragm as determined by the method or apparatus of any of claims 1 to 9.

13. A radiotherapy apparatus comprising a radiation source and a control unit, the source being mounted on a tracking device and being controlled by a control unit to direct the radiation towards the calculated position of the tumor based on the current measurement of diaphragm position obtained by the method or apparatus of any of claims 1 to 9.

14. A method of monitoring respiration by monitoring the movement of a patient's diaphragm using the method or apparatus of any of claims 1 to 9.

15. A method of determining the degree of lung inspiration of a patient substantially as herein described with reference to the accompanying drawings.

16. An apparatus for monitoring the position of a patient's diaphragm substantially as herein described with reference to the accompanying drawings.

Abstract

Respiration Monitor

A respiration monitor comprises a transducer array 5 having a plurality of individual transducer elements 7 that span at least part of the region of diaphragm movement of a patient. A patient 1 having a lung 2 and an abdomen 3 being separated therefrom by a diaphragm 4 is fitted with an ultrasound transducer array 5 over the lung sinus 6 prior to being given a CT or MRI scan. Each individual transducer element 6 emits an ultrasound pulse and then detects its echo in the known manner. Because air has a much higher acoustic impedance than tissue, the reflection of the ultrasound beam is much more pronounced when the lung is insonated.

By measuring the strength of the receiving signal, it is possible to determine to a high degree of accuracy the position of the patient's diaphragm.

Fig. 1

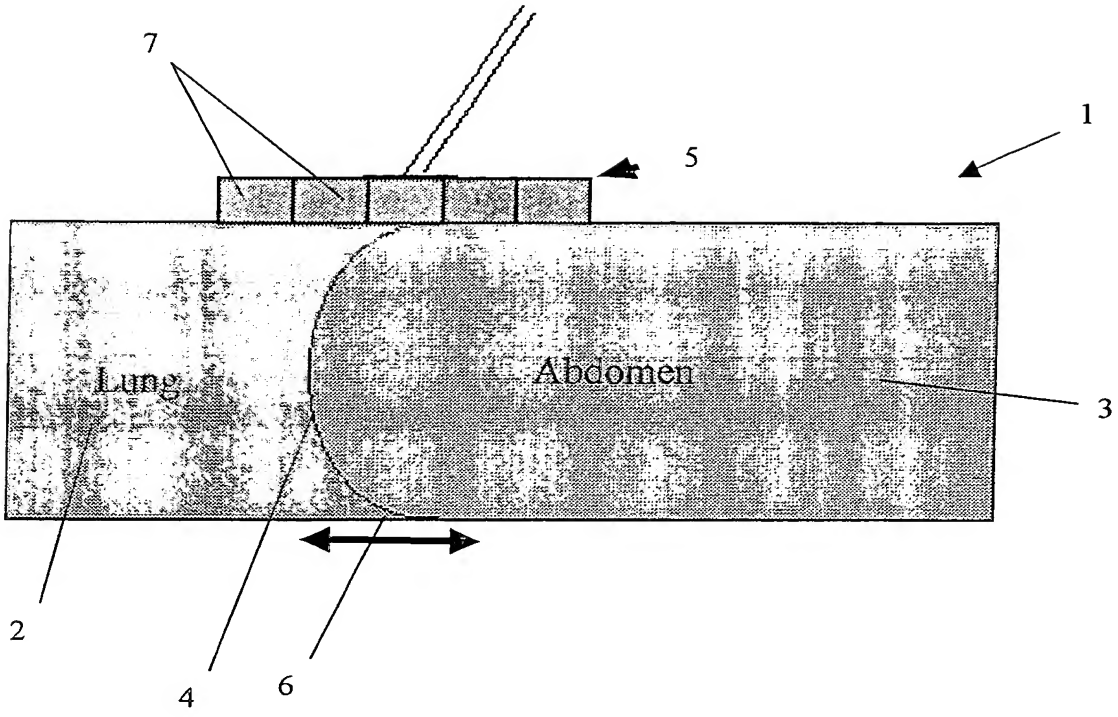


Fig. 2

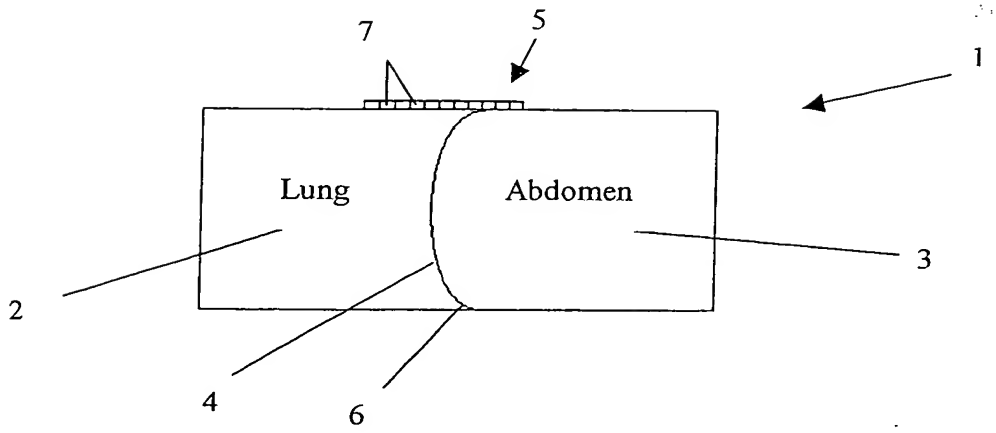


Fig. 3

Fig. 4

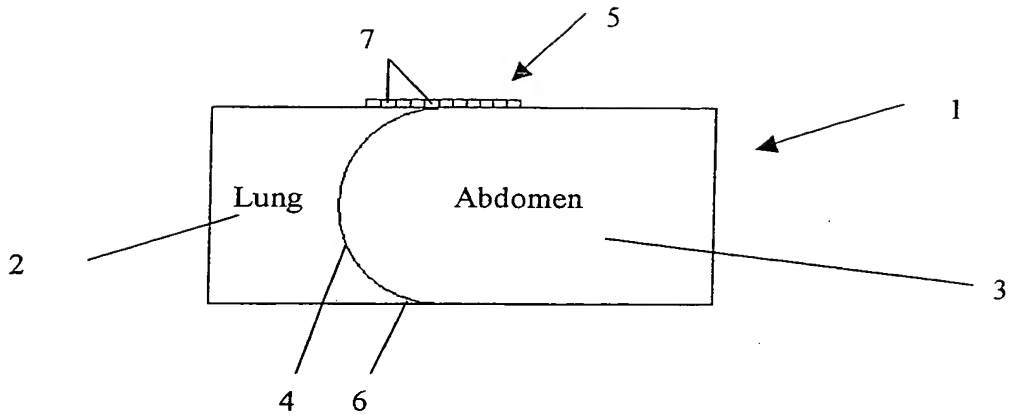


Fig. 5

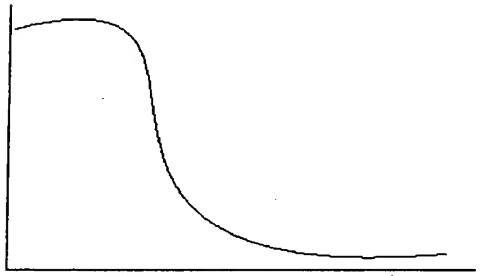
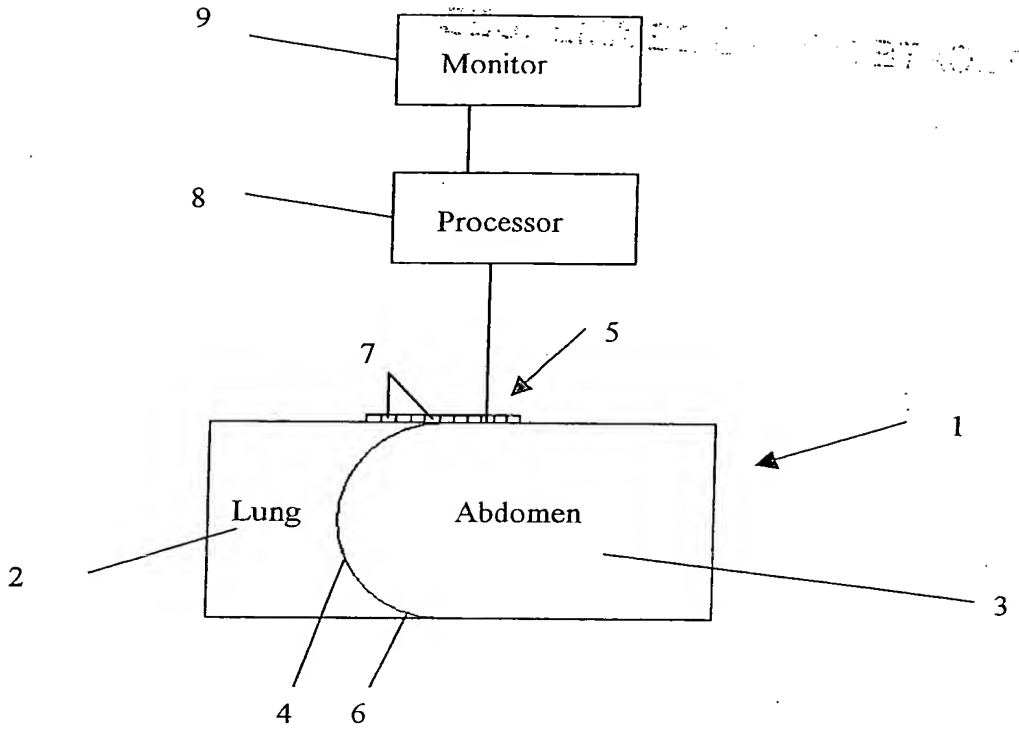


Fig. 6



THIS PAGE BLANK (USPTO)

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.
1300 I Street, N.W.
Washington, D.C. 20005

SERIAL NO: 10/725,431

DOCKET NO: 09032.0001